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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,379	06/04/2001	Bevyn Jarrott	14099	1045

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,379	JARROTT ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,19-21 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23* is/are allowed.

6)☒ Claim(s) *1-6,19-21 and 24-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included amendment to claims 1 and 20, filed on 1/29/2004 is made of record.

Claims 1-6,19-21 and 23-25 are pending

In view of applicants' response, the following apply.

Claim Objections

Claims 1 and 20 are objected to because of the following informalities:

1. Claim 1 recites Markush choices in plural. They should be in singular. As recited they imply mixture of salts, solvates , prodrugs etc.
2. In claim 20, the formula shown is incorrect. The $^{-}CH_3$ group needs to be replaced with $^{-}CH_2$ group.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 19-21 and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. Recitation of "prodrugs" in claim 1 is indefinite as it is not clear what is being claimed. Prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense recitation of

prodrugs is acceptable. However, the definition of optionally substituted group includes various functional groups include such groups, namely esters, alkoxycabonyl etc. and therefore it is not clear what is the difference between these variable groups and the prodrug groups. It is unclear therefore what is a prodrug and what is not a prodrug. Given two ester groups, how would one know which of these ester groups would undergo hydrolysis in vivo to qualify as prodrug? Specification has no guidance as to how would one distinguish the dual definition of the same group and to ascertain which ester is a prodrug group, which ester is not. In short the term "prodrug" as applied instant compounds renders the claim ambiguous. Thus recitation of the term "prodrug" in claim 1 imparts ambiguity to the claim. Prodrugs in general are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense recitation of prodrug is acceptable. However, claim 1 includes ester groups. As prodrugs are suppose to include esters, it s not clear when an ester is prodrug and when an ester is not a prodrug.

In addition, the definition of various variable groups embraced in R^1 and R^2 groups include such groups, namely esters, alkoxycaronyl etc., and again it is not clear what is the difference between these variable groups and the prodrug group.

Furthermore, it is not clear whether compounds bearing these groups are excluded from being potential "prodrug". If compounds bearing these groups, which are likely to undergo in vivo transformation, is excluded then what is included in the

definition of prodrug and where on the compound of formula I, these groups are placed, is not clear.

The issue is how would one know which is prodrug group and which is not, given the fact that various variable groups embraced also includes several such prodrug groups. In addition, a prodrug by definition is not active compound and need to undergo transformation in vivo to active form. If various variable groups embraced were also to be prodrug, then the compounds embraced had to be inactive and therefore issue of enablement as to its utility would arise and method of use claims as well as pharmaceutical composition claims would have be to rejected under 112 first paragraph for lack of scope of enablement.

Hence this rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 19, 21, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. US 3,274,190 for reasons of record. To repeat:

Gray et al. teaches several β-hydroxyphenylethylamino-Het compounds, which include compounds claimed herein, for the relief of pain. Se column 1 and column 2, especially see column 2, for formula shown on line 5 and note the definition of various varible group. Note the definition of Het includes pyrimidine as seen on line 36. Note also on lines 48-64, Gray teaches various substituents and as well as equivalency. See examples 7-40 shown on column 9-19, for various pyrimidine compounds, which includes mono, di and trisubstituted pyrimidine compounds. Note on example 45, Gray teaches an equivalent triazine with diamino groups.

Gray differs from the instant claims in not exemplifying compounds having amino or substituted amino groups on 4 and 6 positions. However, Gray et al. clearly teaches equivalency of the exemplified Het core and the substituents on them shown in the examples with those claimed for the general formula as seen in column 2, lines 33-64.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in pyrimidine ring taught in the examples 7-40 and the aryl ring as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Applicants' traversal of this rejection after amending the claims to exclude amino group, is not persuasive. Applicants argue that teaching of Gray et al. is limited to NH_2 group and that Gray et al. does not teach substituted amino group. This is deemed as not persuasive. One trained in the art would know that Gray et al. teaches a generic substituents on the heteroaryl ring as seen in lines 48-64 and therefore would be motivated select even substituted amino groups. See Ex parte Weston 121 USPQ 428; In re Doebel 174 USPQ 156.

Hence this rejection is deemed as proper and is maintained.

Allowable Subject Matter

Claim 23 is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (571) 272-0674. If Applicants are unable to reach Mukund Shah within 24-hour period, they may contact James O. Wilson, Acting-SPE of art unit 1624 at 571-272-0661.

The fax phone number for the organization where this application or proceeding is assigned (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

V. Balasubramanian
Venkataraman Balasubramanian

6/12/2004